FILED: Page 13

Herewith

## **AMENDMENTS TO THE CLAIMS**

Please cancel claims 1-27. Please add new claims 28-69 as follows:

Claims 1-27 (Cancelled)

28. (New) A method for targeting a compound to a cell undergoing perturbation of the normal organization of its plasma membrane (PNOM-cell), comprising the steps of:

(i) contacting a cell population comprising said PNOM-cell with a compound or a conjugate comprising said compound, wherein said compound is represented by the structure as set forth in formula (I):

HO 
$$\longrightarrow$$
 OH
$$R' \qquad R \qquad (CH_2)_n M \longrightarrow (CH_2)_m D$$
(I)

including pharmaceutically acceptable salts, metal chelates, solvates and hydrates of the compound represented by the structure as set forth in formula (I), and solvates and hydrates of the salts; wherein each of R and R' groups is independently selected at each occurrence from hydrogen,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ ,  $C_9$ ,  $C_{10}$ ,  $C_{11}$ ,  $C_{12}$ ,  $C_{13}$ ,  $C_{14}$ ,  $C_{15}$  or  $C_{16}$  linear or branched alkyl, linear or branched hydroxy-alkyl, linear or branched fluoroalkyl, aryl or heteroaryl composed of one or two rings, or combinations thereof; n and m each stands independently for an integer of 0, 1, 2, 3 or 4; n and m may be the same or different; M is selected from null, -O-, -S-, and -N(U), wherein U stands for hydrogen, or  $C_1$ ,  $C_2$ ,  $C_3$ , or  $C_4$  alkyl; x and z each being an integer of 0, 1 or 2, where x and z can be the same or different; y is an integer of 0, 1 or 2; where in the case that y=2, the

FILED:

Herewith

Page 14

substituent R' may be the same or different at each occurrence; and D is a marker for diagnostics, hydrogen, hydroxyl, F or a drug;

(ii) thereby targeting said compound to said PNOM-cell within said cell population.

29. (New) A method according to Claim 28, wherein D is a marker for diagnostics or a drug.

30. (New) A method according to Claim 29, wherein M is null.

31. (New) A method according to Claim 28, comprising the steps of:

(i) contacting a cell population comprising said PNOM-cell with a compound or a conjugate comprising said compound, wherein said compound is represented by the structure as set forth in formula (II):

II

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (II) and solvates and hydrates of the salts; wherein R represents hydrogen or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub>, C<sub>10</sub>, C<sub>11</sub>, C<sub>12</sub>, C<sub>13</sub>, C<sub>14</sub>, C<sub>15</sub> or C<sub>16</sub> linear or branched alkyl, linear or branched hydroxyalkyl, linear or branched fluoro-alkyl, aryl or heteroaryl composed of one or two rings, or combinations thereof; n and m each stands independently for an integer of 0, 1, 2, 3 or 4; n and m may be same or different; M is selected from null, -O-, -S- and -N(U), wherein U stands for hydrogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, or C<sub>4</sub> alkyl; D is a marker for diagnostics, hydrogen or a drug;

FILED:

Herewith

Page 15

(ii) thereby targeting said compound to said PNOM-cell within said cell population.

32. (New) A compound represented by the structure as set forth in formula II, wherein D is a marker for diagnostics or a drug.

33. (New) A compound according to Claim 32, wherein M is null.

34. (New) A compound represented by the structure as set forth in formula II, wherein R is C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> linear or branched fluoro-alkyl, or linear or branched hydroxy-alkyl; M is null, and D is hydrogen.

35. (New) A compound represented by the structure as set forth in formula (III):

Ш

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (III) and solvates and hydrates of the salts; wherein  $R^3$  is hydroxyl or F;  $R^4$  is selected from  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ ,  $C_9$  or  $C_{10}$  linear or branched alkyl, and k is an integer selected from 0, 1, 2, 3, 4 and 5.

36. (New) A compound represented by the structure as set forth in formula (IV):

FILED:

Herewith

Page 16

IV

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (IV) and solvates and hydrates of said salts.

## 37. (New) A compound represented by the structure as set forth in formula (V):

ν

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (V) and solvates and hydrates of the salts; wherein J is selected from F and OH, and r stands for an integer of 4,5,6,7,8,9 or 10.

38. (New) A compound according to Claim 37, wherein r is 5 and J is F.

FILED:

Herewith

Page 17

39. (New) A compound according to Claim 37, wherein r is 4 and J is F.

40. (New) A compound according to Claim 34, represented by the structure as set forth in formula (VI):

VI

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (VI) and solvates and hydrates of said salts; wherein J is selected from hydrogen, F and OH.

41. (New) A compound represented by the structure set forth in formula (VII):

VII

including pharmaceutically acceptable salts, hydrates and solvates of the compound represented by the structure as set forth in formula (VII) and solvates and hydrates of said salts, wherein Q is selected from technetium, oxo-technetium, rhenium and oxo-rhenium,

FILED: Herewith

Page 18

 $R^4$  is selected from hydrogen,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , and  $C_6$  linear or branched alkyl, and p stands for an integer, selected from 1, 2, 3, 4 and 5.

42. (New) A compound according to Claim 32 represented by the structure set forth in formula (IX):

HO 
$$R^5$$
  $OH$   $OH$ 

IX

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (IX) and solvates and hydrates of said salts; wherein  $R^5$  is selected from hydrogen,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , or  $C_6$  linear or branched alkyl,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , or  $C_6$  linear or branched fluoro-alkyl, and  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , or  $C_6$  linear or branched hydroxy-alkyl; q stands for an integer selected from 1, 2, 3, 4 and 5; and Y is a marker for fluorescence.

43. (New) A compound according to Claim 42, wherein R<sup>5</sup> is CH<sub>3</sub>; q is selected from 3, 4, and 5 and Y is a marker for fluorescence.

44. (New) A compound according to Claim 42, represented by the structure as set forth in formula (X):

APPLICANT(S): ZIV, Ilan et al.

Not yet assigned

SERIAL NO.: FILED:

Herewith

Page 19

X

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (X) and solvates and hydrates of said salts.

45. (New) A method according to Claim 31, wherein said compound is represented by the structure as set forth in formula (XI):

 $\mathbf{XI}$ 

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (XI) and solvates and hydrates of the salts; wherein R represents hydrogen or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> C<sub>10</sub>, C<sub>11</sub>, C<sub>12</sub>, C<sub>13</sub>, C<sub>14</sub>, C<sub>15</sub> or C<sub>16</sub> linear or branched alkyl, linear or branched hydroxyalkyl, linear or branched fluoro-alkyl, aryl or heteroaryl composed of one or two rings, or combinations thereof.

46. (New) A compound as represented by the structure set forth in formula XI, wherein R represents C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> linear or branched alkyl, including pharmaceutically acceptable salts, hydrates, solvates and chelates, wherein F is <sup>18</sup>F or <sup>19</sup>F.

FILED:

Herewith

Page 20

47. (New) A compound according to Claim 32 represented by the structure set forth in formula (XIII):

IIIX

including pharmaceutically acceptable salts hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (XIII) and solvates and hydrates of the salts; R represents hydrogen or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub>, C<sub>10</sub>, C<sub>11</sub>, C<sub>12</sub>, C<sub>13</sub>, C<sub>14</sub>, C<sub>15</sub> or C<sub>16</sub> linear or branched alkyl, linear or branched hydroxy-alkyl, linear or branched fluoro-alkyl, aryl or heteroaryl composed of one or two rings, or combinations thereof; m stands for an integer of 0, 1, 2, 3 or 4; D is a marker for diagnostics or a drug to be targeted to PNOM-cells.

48. (New) A compound according to Claim 47, wherein R represents hydrogen or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ ,  $C_9$ ,  $C_{10}$ ,  $C_{11}$ ,  $C_{12}$ ,  $C_{13}$ ,  $C_{14}$ ,  $C_{15}$  or  $C_{16}$  linear or branched alkyl; m is an integer of 2 and D is <sup>18</sup>F.

49. (New) A compound according to Claim 47 represented by the structure set forth in formula (XIV):

FILED: Herewith

Page 21

## XIV

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (XIV) and solvates and hydrates of the salts; wherein F may be <sup>18</sup>F or <sup>19</sup>F.

50. (New) A compound according to the structure set forth in any of the formulae III, IV, V, VI, VII, IX, X, XI, XIII, or XIV, comprising or being linked to a marker for imaging.

51. (New) A compound of according to Claim 50, wherein said marker for imaging is Tc, Tc=O, In, Cu, Ga, Xe, Tl, Re and Re=O, <sup>123</sup>I, <sup>131</sup>I, Gd(III), Fe(III), Fe<sub>2</sub>O<sub>3</sub>, Fe<sub>3</sub>O<sub>4</sub>, Mn(II) <sup>18</sup>F, <sup>15</sup>O, <sup>18</sup>O, <sup>11</sup>C, <sup>13</sup>C, <sup>124</sup>I, <sup>13</sup>N, <sup>75</sup>Br, Tc-99m or In-111.

52. (New) A compound of according to Claim 32, wherein said marker for diagnostics is Tc, Tc=O, In, Cu, Ga, Xe, Tl, Re and Re=O, <sup>123</sup>I, <sup>131</sup>I, Gd(III), Fe(III), Fe<sub>2</sub>O<sub>3</sub>, Fe<sub>3</sub>O<sub>4</sub>, Mn(II) <sup>18</sup>F, <sup>15</sup>O, <sup>18</sup>O, <sup>11</sup>C, <sup>13</sup>C, <sup>124</sup>I, <sup>13</sup>N, <sup>75</sup>Br, Tc-99m or In-111.

APPLICANT(S): ZIV, Ilan et al. SERIAL NO.:

Not yet assigned

FILED:

Herewith

Page 22

A compound according to Claim 50, wherein said marker for imaging is 53. (New)

detectable by a detector of color, fluorescence, x-ray, CT scan, magnetic resonance

imaging (MRI), radio-isotope scan, single photon emission tomography (SPECT) or

positron emission tomography (PET).

A compound according to Claim 32, wherein said marker for diagnostics is 54. (New)

detectable by a detector of color, fluorescence, x-ray, CT scan, magnetic resonance

imaging (MRI), radio-isotope scan, single photon emission tomography (SPECT) or

positron emission tomography (PET).

55. (New) A pharmaceutical or a diagnostic composition, comprising as an active

ingredient an effective amount of a compound according to the structure set forth in any

of the formulae III, IV, V, VI, VII, IX, X, XIII, or XIV and a pharmaceutically or

diagnostically acceptable carrier.

56. (New) A method for targeting a compound to a cell undergoing perturbation of

the normal organization of its plasma membrane (PNOM-cell), comprising the steps of:

(i) contacting the cell population comprising said PNOM-cell with a compound

represented by the structure set forth in any of the formulae III, IV, V, VI, VII, IX, X, XI,

XIII, or XIV or a pharmaceutical composition comprising said compound;

(ii) thereby targeting said compound to said PNOM-cell within said cell population.

57. (New) A method according to Claim 56, wherein said PNOM-cell is a cell

undergoing a cell death process.

58. (New) A method according to Claim 28, wherein said PNOM-cell is a cell

undergoing a cell death process.

22

APPLICANT(S): ZIV, Ilan et al. SERIAL NO.:

Not yet assigned

FILED:

Herewith

Page 23

- A method according to Claim 31, wherein said PNOM-cell is a cell 59. (New) undergoing a cell death process.
- 60. (New) A method according to Claim 57, wherein said cell death process is apoptosis.
- 61. (New) A method according to Claim 58, wherein said cell death process is apoptosis.
- 62. (New) A method according to Claim 59, wherein said cell death process is apoptosis.
- 63. (New) A method for detecting a PNOM-cell within a cell population, said method comprising:
- (i) contacting the cell population with a compound or a pharmaceutical composition comprising said compound, wherein said compound is represented by the structure set forth in any of formulae I, II, III, IV, V, VI, VII, IX, X, XI, XIII, or XIV, comprising or being linked to a marker for diagnostics; and
- (ii) determining the amount of said compound bound to said cells, wherein detection of a significant amount of said compound bound to a cell indicates its being a PNOM-cell.
- 64. (New) A method for imaging PNOM-cells in a subject, human or an animal, comprising:
- (i) administering to said subject, human or an animal a compound or a pharmaceutical composition comprising said compound wherein said compound is represented by the structure set forth in any one of formulae I, II, III, IV, V, VI, VII, IX, X, XI, XIII, or XIV, comprising or being linked to a marker for imaging; and

APPLICANT(S): ZIV, Ilan et al.

Not yet assigned

SERIAL NO.: FILED:

Herewith

Page 24

(ii) imaging the human or animal, so as determine the amount of said pharmaceutical composition or said compound bound to cells, wherein imaging of a significant amount

of said compound bound to cells indicates their being PNOM-cells.

65. (New) The method of Claim 64 for determining of a disease process, a focus of

tumor, or a response to treatment of a disease, in a human or non-human subject,

wherein said disease process, focus of tumor, or response to treatment is associated with

occurrence of cells undergoing a cell death process.

66. (New) A method according to Claim 65, wherein said cell death process is

apoptosis.

67. (New) A method for targeting a cytotoxic drug to a tumor which has cells

undergoing cell death, said method comprising the step of administering a compound as

represented by a structure set forth in any of the formulae I, II, III, IV, V, VI, VII, IX, X,

XI, XIII, or XIV, comprising or being linked to the cytotoxic drug, thereby targeting of

the cytotoxic drug to the cells undergoing cell death within the tumor.

68. (New) A PMBC-PET precursor, represented by a structure as set forth in any of

the formulae I, II, III, V, VI, IX, X, XI, XIII or XIV, comprising or being linked to a

moiety to be substituted by an <sup>18</sup>F radio-isotope upon radio-labeling, thereby generating an

<sup>18</sup>F-labeled compound.

69. (New) A PMBC-PET precursor according to Claim 68, wherein said moiety is a

sulfonate, a nitro, a halogen, or a hydroxyl group.

24